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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,896	08/08/2001	Dennis W. Metzger	1954.1002-009	3394

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,896	METZGER ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *1-7,9-15,17-19,21-23 and 25-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8,16,20,24 and 30-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' amendment filed 10-2-03 has been entered. Claims 8, 16, 20 and 24 have been amended. Claims 30-45 have been added. Claims 1-45 are pending and claims 8, 16, 20, 24 and 30-45 are under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 8, 16, 20 and 24 remain rejected and claims 30-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention and is repeated for the reasons set forth in the preceding Official action mailed 3-28-03 (Paper No. 8). Applicant's arguments filed 10-2-03 have been fully considered but they are not persuasive.

Claims 30-45 are newly added claims. Claims 30-35 depend on claim 8. Claims 36-41 depend on claim 16. Claims 42 and 42 depend on claim 20. Claims 44 and 45 depend on claim 24. The newly added claims 30-45 specify the T-cell independent antigen as a carbohydrate antigen, lipid antigen, a carrier conjugate antigen, a lipopolysaccharide antigen, or a phage antigen, and the immune response is a humoral immune response that enhances IgG2a and UgG3 antibody response.

Applicants cite references Tahara et al. (exhibit A), Rakhmilevich et al. (exhibit B), Kim et al. (exhibit C), Jiang et al. (exhibit D), and Watanabe et al. (exhibit E) and argue that the specification provides guidance for how to administer polynucleotide encoding IL-12 and/or TI antigen in vivo and the art teach how to make the expression vector expressing IL-12 (amendment, p. 8-11). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 3-28-03 (Paper No. 8). Tahara and Jiang (exhibits A and D) teaches using cells transfected with retroviral vector expressing IL-12 for anti-tumor effect in mice. Delivery of cell in vivo to stimulate an immune response for anti-tumor effect is different from delivery of a polynucleotide in vivo to stimulate an immune response for therapeutic effects in vivo because the proteins have been expressed in the transfected cells before being released in the target site, however, the polynucleotide has to be delivered to the target site and sufficient amount of protein, such as IL-12 protein, has to be expressed to stimulate or enhance immune response in vivo.

Kim (exhibit C) teaches codelivery of genes for IL-12 and GM-CSF along with DNA vaccine formulation for HIV-1 antigen and codelivery of IL-12 gene results in reduction of specific antibody response, while codelivery of GM-CSF genes results in enhancement of specific antibody response, and a dramatic increase in specific CTL response from the mice coimmunized of both HIV-1 DNA vaccine and IL-12 genes (e.g. abstract). The present invention is directed to the use of IL-12 polynucleotide and T-cell independent antigen which is an antigen that is capable of inducing immune response without the need of mature T cells and the TI antigen includes carbohydrates,lipids, glycolipids, lipopolysaccharide, and phages etc. The hard copies of the references submitted are in bad conditions such that several areas of the references

are not readable and examiner has a hard time to comprehend the articles, for example, how the IL-12 genes is administered in vivo in Kim reference. Despite the unclearness of Kim reference, the HIV-1 DNA vaccine stimulates immune response from T cells, therefore, the HIV-1 DNA vaccine is not a TI antigen and the subject matter taught by Kim is different from that of the present invention. Further, TI antigens are relatively poor immunogen (specification, p. 1) and the IL-12 polynucleotide has to be delivered to the target site and sufficient amount of protein, such as IL-12 protein, has to be expressed to stimulate or enhance immune response in vivo. As discussed in the preceding Official action mailed 3-28-03 (Paper No. 8), gene delivery in vivo was unpredictable at the time of the invention, whether sufficient polynucleotides can be delivered to the target site and whether sufficient proteins are expressed to stimulate immune response depend on the administration routes, for example, oral administration, intravenous administration, or topical administration on skin of the IL-12 gene and TI antigen may not stimulate or enhance immune response in vivo.

Rakhmilevich and Watanabe (exhibits B and E) teaches intradermal injection of IL-12 DNA for anti-tumor effects and systemic NK cell activation and Th1 response in vivo, respectively. As discussed above, TI antigens are relatively poor immunogen (specification, p. 1) and the IL-12 polynucleotide has to be delivered to the target site and sufficient amount of protein, such as IL-12 protein, has to be expressed to stimulate or enhance immune response in vivo. As discussed in the preceding Official action mailed 3-28-03 (Paper No. 8), gene delivery in vivo was unpredictable at the time of the invention, whether sufficient polynucleotides can be delivered to the target site and whether sufficient proteins are expressed to stimulate immune response depend on the administration routes, for example, oral administration, intravenous

administration, or topical administration on skin of the IL-12 gene and TI antigen may not stimulate or enhance immune response in vivo. The specification must provide sufficient enabling disclosures for the full scope of the invention claimed but fails to do so.

Applicants argue that the references cited by examiner are irrelevant to the claimed invention and they do not cast doubt on applicants' claimed method of inducing or enhancing an immune response for a T-cell independent antigen in vivo (amendment, p. 11-13). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 3-28-03 (Paper No. 8) and the reasons set forth above. Although the teachings of the cited references do not relate to stimulating immune response with IL-12 DNA and Ti antigen in vivo, the teachings of the cited references do teach the unpredictability of gene transfer in vivo, which is required in the present invention to deliver IL-12 DNA and TI antigen via various administration routes so as to stimulate or enhance immune response in a host, for example, oral administration, intravenous administration, or topical administration on skin of the IL-12 gene and TI antigen may not stimulate or enhance immune response in vivo. Thus, one skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed.

Conclusion

No claim is allowed.

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. Due to the move of USPTO to new site in Alexandria, Virginia, examiner's telephone number will be changed to (571) 272-0726 **after January 12, 2004**. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

S Chen

Shin-Lin Chen, Ph.D.